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Therapeutic Value of the Mixed Toxins of the Streptococcus of Erysipelas and Bacillus Prodigiosus in the Treatment of Inoperable Malignant Tumors.

With a Report of 160 Cases.

BY

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THE THERAPEUTIC VALUE

OF THE

MIXED TOXINS OF THE STREPTOCOCCUS OF ERYSIPELAS AND BACILLUS PRODIGIOSUS IN THE TREATMENT OF INOPERABLE MALIGNANT TUMORS,

WITH A REPORT OF ONE HUNDRED AND SIXTY CASES.[1]

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In a series of papers already published[2] I have reported the results of my investigations concerning the action of the streptococcus of erysipelas and its toxins upon inoperable malignant tumors. In the earlier papers an attempt was made to set forth the clinical and experimental evidence then existing in support of the view that an attack of erysipelas occurring by accident, or brought about by inoculation, in a patient suffering from malignant disease, not infrequently produced marked improvement, and in some cases permanent cure. It is unnecessary to go again over the ground, and it is sufficient to state that a considerable number of cases reported by competent observers, of undoubtedly malignant tumors, have been permanently cured by an attack of erysipelas. Czerny has recently added two most important observations bearing upon this question.

The seven observations of Fehleisen, in which he produced erysipelas by inoculation—in one of which the tumor disappeared entirely, and nearly all of which showed improvement—furnish additional evidence

[1] Read before the Johns Hopkins Medical Society, April 6, 1896.

[2] Annals of Surgery, September, 1891. The American Journal of the Medical Sciences, May and July, 1893; ibid., July, 1894. N. Y. Med. Record, January 19, 1895.

in support of the view that the streptococcus of erysipelas has in it some quality that exerts an antagonistic influence upon the cells of malignant tumors.

The case that led me to take up these investigations was one of small round-celled sarcoma of the neck, which had been operated upon by Dr. William T. Bull five times at the New York Hospital. At the last operation, in 1884, it was found impossible to remove the growth. The patient was given up as hopeless. A few days later an attack of erysipelas occurred, followed by a second attack shortly after the first had subsided. The tumor entirely disappeared. I was able to trace the patient and found him alive and quite free from recurrence in 1891, seven years afterward.

My first experiments were conducted with repeated injections of living bouillon-cultures of the streptococcus of erysipelas, introduced into the substance of the tumor, and the results in a series of ten cases were brought before the Surgical Section of the New York Academy of Medicine in December, 1892. Two of these cases, both inoperable, hopeless cases of recurrent sarcoma, are alive and well, one more than three years, and the other more than four years after treatment. The unmistakable improvement that followed the repeated injections even when no erysipelas was produced—especially in sarcoma—led me to believe that a portion, if not all, of the curative influence might be due to the toxins, rather than to the action of the germ itself.

This point was one that could be easily determined by experiment. The great advantages of the toxins over the living cultures were at once apparent. First, the element of danger, which was not inconsiderable, I myself having had two deaths from inoculating the living germ, was eliminated. Secondly, it was possible to regulate with some degree of accuracy the dose of the toxins, a thing quite impossible when using living cultures. Furthermore, my own experience, as well as that of others, had proved that it was often extremely difficult and sometimes impossible to produce erysipelas even with very virulent cultures.

In my first experiments with the toxins (in 1892) I simply sterilized the bouillon-cultures by heating them to 100° C., and then injected them into the substance of the tumor. The symptoms and reaction corresponded almost exactly with those following the use of the living cultures, though they were less severe and shorter in duration.

Knowing that the action of heat produced certain chemical changes in the toxic products of bacteria, I next used the soluble products by passing the living bouillon-cultures through a Kitasato filter and using the filtrate. The reaction was similar to that described following injections of the living cultures, but decidedly less severe and less persistent. The local redness and induration were also much less marked. The effect on the tumors, especially sarcoma, was to inhibit

the growth, and in some cases to diminish the size. The solution was so weak that it required very large doses, 2 to 4 c.c., to produce much reaction.

In order to increase the virulence of the cultures and the strength of the toxins I made use of the principle demonstrated by Roger, of Paris, that the bacillus prodigiosus, a non-pathogenic organism, has the power to intensify certain pathogenic germs, notably erysipelas. As far as I am aware, no one had tried a combination of erysipelas streptococcus with any other germ, or their mixed toxins in the human being, nor had the idea ever been suggested in connection with the treatment of malignant tumors. With the valuable aid of Dr. Alexander Lambert, at that time Fellow in Bacteriology at the College of Physicians and Surgeons, a filtrate containing the soluble toxic products of the streptococcus of erysipelas (obtained from a fatal case) and another containing the soluble products of the bacillus prodigiosus were prepared. These solutions were sterilized by filtration without the use of heat, and preserved in glass-stoppered bottles by the addition of thymol crystals.

The two solutions were mixed at the time of using in about the proportion of one part of the bacillus prodigiosus toxin to four or five parts of the erysipelas-toxin. The reaction that followed was much more severe — a chill coming on in one-half hour to an hour after the injection, and lasting fifteen to forty-five minutes. Nausea, vomiting, severe headache, with temperature 103° to 104°, usually followed an injection of ♏ ij to iv of the bacillus prodigiosus toxins, with ♏ viij to xvj of the erysipelas-toxins. The reaction and disagreeable symptoms usually subsided within twelve hours, but not infrequently a marked herpes labialis followed. The effect upon the tumors was much more marked than when the erysipelas-toxins alone were used.

A little later, at the suggestion of Mr. B. H. Buxton, Director of the Loomis Laboratory (without whose untiring zeal and unremitting assistance during the past three years much of this work would have been impossible), the two germs were grown together in the same broth, the erysipelas streptococcus being first grown alone for ten days, the prodigiosus-toxin then added, and the two allowed to grow together for ten days. The results showed this to be a further improvement in technique. Two years ago I made another change, with a view to utilize whatever of value might exist in the toxins contained in the dead germs themselves. The cultures were heated to a temperature sufficient to render them sterile (which was found to be 58° to 60° C.) for one hour, and then used without filtration. This preparation proved to be by far the strongest, and experience has shown it to be superior to the filtered solution in its action upon malignant tumors.

The value of all the preparations of the toxins has been found to depend largely upon the virulence of the original cultures employed, and in the successful cases the toxins were all made from cultures obtained from

fatal cases of erysipelas. The culture gradually loses its virulence after a few generations, and various means were used to restore it, the most efficient being to pass the culture through a series of rabbits. Marmorek, at the Pasteur Institute in Paris, has succeeded in developing a remarkable degree of virulence in the streptococcus by this method. The most powerful preparation of the mixed toxins that Mr. Buxton has been able to make produced very severe constitutional symptoms, with a prolonged chill and a temperature of 104½° in doses of one-half a minim (0.066 c.cm.).

It is very important to remember that much larger quantities can be borne when injected subcutaneously than when injected directly into a vascular tumor, the difference being undoubtedly due to the more rapid absorption in the latter instance.

I have adopted the plan of beginning with a very small dose—*e. g.*, one minim of the filtrate, or one-half a minim of the unfiltered toxins—and gradually increasing the dose each day until the reaction-temperature reaches 103° to 104° F. The temperature has been the chief guide in estimating the dose, and very little benefit has been noted in cases in which no reaction was obtained. The frequency of the injections has depended upon the general condition of the patient and upon the rapidity of recovery from the depression of the preceding dose.

Usually the injections have been given daily, aiming to get two or three well-marked reactions during a week. If well borne, the treatment has been continued from two to three weeks, and if at the end of that time no decided improvement has taken place, it has been discontinued. In some of the successful cases it has been kept up for three or four months, occasional intervals of a few days' rest having been allowed. In several instances, in spite of the reaction and depressing effects, the patients have steadily improved in general condition and have gained markedly in weight.

With this brief *résumé* of the method of preparation, let us proceed to an analysis of the cases treated, which form the basis of the present paper. There are three important questions which a careful study of these cases ought to enable us to answer:

First. Have these toxins any antagonistic or beneficial influence upon malignant tumors?

Secondly. If so, in what varieties of tumors is this influence most marked?

Thirdly. Is this action permanent in character or merely temporary?

Grouping the cases according to their several varieties we have: Sarcoma, 94; round-celled, 52; spindle-celled, 14; melanotic, 7; chondro-sarcoma, 2; sarcoma, special type of cell not stated, 8. Carcinoma, including epithelioma, 63; of breast, 31; of uterus, 3; of cheek, 4; of

sternum (secondary), 1; of tongue, 4; of neck, 3; of rectum, 3; of lip, 2; sarcoma or carcinoma, 10 cases.

In addition to the above cases of malignant tumors eight other cases have been treated with the toxins. These were as follows: tubercular-2 cases; keloid, 1; goitre, 2; recurrent fibro-angeioma, 1; mycosis fun, goïdes, 1; fibroma, 1.

Of the cases of sarcoma, forty-five, or more than one-half, showed more or less improvement. The variety that showed the greatest improvement was the spindle-celled sarcoma; that which showed the least was the melanotic. Next to the spindle-celled, in the order of benefit, was the mixed-celled, round- and spindle-, then round-celled; while osteosarcoma closely approached the melanotic in showing but little effect of the toxins. In a series of seven cases of melanotic sarcoma no improvement was observed in five cases, and very slight change in the two others. It should be observed, however, that in most of these cases the tumors were multiple and the disease thoroughly generalized before treatment was begun. Yet, in all these cases the antagonistic action of the toxins was so trifling that, were it not for the fact that at least one case of melanotic sarcoma has been cured by accidental erysipelas, there would be little to encourage one to a further trial of the toxins in this class of cases.

With osteosarcoma the results are scarcely more satisfactory. Most of the cases showed slight improvement; one case, a very large osteo-chondrosarcoma was apparently cured, remained well for nearly a year, and then recurred. Further treatment caused temporary improvement, but the patient has since been slowly getting worse, and a fatal termination will undoubtedly occur. This case is very important on account of the size of the original tumor. The fact that it recurred after it had been once apparently cured renders the diagnosis absolutely certain.

In one case of round-celled sarcoma of the neck, of very rapid growth, the tumor decreased from the size of an orange to the size of a hen's egg in one week, after three injections of the mixed toxins. No further reduction took place, and in spite of large doses of the toxins the tumor again began to increase rapidly in size and caused death within three months. In many of the other cases of round-celled sarcoma the improvement was very striking, but in only two cases of purely round-celled sarcoma did a cure result.

In one case of round-, spindle-, and oval-celled sarcoma (recurrent) the tumors disappeared, and the patient is alive and well more than three years after treatment.

The spindle-celled variety, though embracing a small proportion of the total number of sarcoma cases, forms by far the largest proportion of successful cases. The reason for this remarkable difference in the action of the toxins upon the different types of sarcoma is not apparent, but an attempt to explain it will be made later on.

Carcinoma. I have thus far been extremely conservative in advocating the toxins in anything but inoperable sarcoma, though I have been steadily experimenting upon carcinoma. My results in carcinoma, while far from ideal, are still such as to lend encouragement to the belief that we are working along the right lines, and that at no very distant day we shall attain in carcinoma some measure of the success that has already been achieved in sarcoma.

The number of cases of demonstrated carcinoma that have been permanently cured by accidental erysipelas would seem to give additional weight to this view. I believe that we have in the toxins nearly, if not quite, all the virtue that exists in the living germ and in a form that can be utilized without risk to the patient.

I have seen undoubted improvement follow the injections of the toxins in a considerable number of cases of inoperable carcinoma. In two cases the tumors disappeared and the patients are at present well, one a year and nine months after treatment, and the other a year. A third case of rapidly growing, twice recurrent carcinoma of the breast, in which a large gland the size of a hickory-nut, encircling the axillary vessels high up, was left at the last operation, February, 1895, has shown very markedly the controlling and inhibiting action of the toxins. In April, 1895, the tumor had recurred in the cicatrix, measured one and a half by two and a half inches, and was growing rapidly. The pectoral muscle was hard and infiltrated. The patient has had the toxins three times a week since, or more than a year. The ulcerated carcinomatous base has been excised once since, but recurred in a few weeks. The induration in the pectoral muscle has nearly disappeared. The diseased gland left in the axilla cannot be felt, and there is no swelling of the arm. The patient weighs ten pounds more than a year ago, and is apparently well at present, June 9, 1896.

This case is not cited as even a probable cure, but simply to show in a striking way the influence of the toxins upon a rapidly growing, recurrent carcinoma, the diagnosis of which has been confirmed by several microscopical examinations.

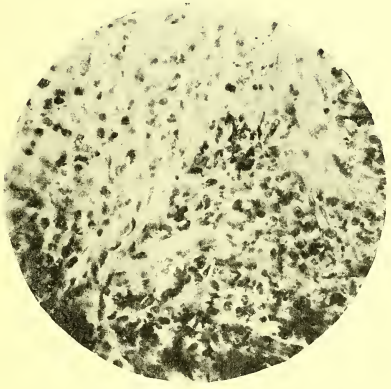
I believe that the chief value of the toxins in carcinoma will probably be found in their use after a primary operation to lessen the chances of recurrence. This is a question that can only be settled by several years of experiment. It seems, however, reasonable to believe that the toxins would have a far better chance to destroy the invisible traces of infection left behind after operation, than after a palpable tumor has developed. One surgeon has written me that he operated upon three cases of advanced carcinoma of the breast in which erysipelas developed during the wound-healing. In no case did recurrence follow, and the cases were traced for a long period—five to fifteen years.

Let us now turn to the third and by far the most important question, Is the action of the toxins permanent—that is, really curative—or not? It is evident that only cases that have remained well for a considerable length of time can be considered in answering this question. Four cases, all pronounced inoperable by well-known surgeons, and in every one of which the diagnosis was confirmed by careful microscopical examination by competent pathologists, are at present well and free from recurrence two and one-half to four and one-half years after treatment. It would seem proper to regard these cases as permanently cured. The oldest case cannot strictly be classed as a cure from the toxins alone, because living cultures were used. Yet this case is, I believe, the only one on record cured by artificially produced erysipelas that has been traced beyond one year. These four cases alone, which were completely hopeless, are, I think, sufficient to demonstrate the curative power of the streptococcus and its toxins upon sarcoma.

The most important cases are reported with some detail, and the remainder summarized.

Case I. *A twice recurrent inoperable sarcoma of the neck with large secondary sarcoma of tonsil; treated with repeated injections of living cultures of erysipelas for four months; well four years after treatment.*—The patient had been operated upon twice by Professor Durante of Rome, and last by Dr. W. T. Bull at the New York Hospital in March, 1891. The tumor of the neck was so large that only a portion could be removed, and the general condition of the patient when I began treatment, May 4, 1891, was so bad that he was expected to live but a short time. The tonsillar tumor was so large that it was impossible to swallow solid food, and liquid food was taken with difficulty.

Fig. 1.



Case I.—Myxosarcoma.

From May 4 to October, 1891, I treated the patient with repeated local injections of living bouillon cultures of the streptococcus of erysipelas. No attack of erysipelas occurred until October, yet improvement followed the injections, and whenever they were discontinued the growth increased in size.

On October 8th a severe attack of erysipelas followed the injection of a new and more virulent culture. During this attack the tumor of the neck nearly disappeared, the tumor of the tonsil decreased in size, and the general condition of the patient rapidly improved until he had regained his usual health and strength. He has had no treatment since October 8, 1891, and he was in good health in October, 1895. He has been repeatedly examined by myself and other surgeons. My last examination, made in September, 1895, showed a small mass at the site of the old scars upon the neck, apparently made up of cicatricial and fibrous tissue. It had remained unchanged for four years. The tumor of the tonsil was still present, though it had apparently shrunken some in size, and the features of malignancy must have been either entirely lost or in complete abeyance. The general condition was excellent.

FIG. 2.



CASE I.—Inoperable sarcoma of neck—melanotic. Slight improvement, temporary.

[Copy from Records, N. Y. Hospital Laboratory.]

Specimen No. 1870. *Microscopical examination and report.* "Operation, a piece of tumor about the size of an orange was removed, but a portion yet remains, being too deeply seated for extermination.

"Microscopically the tumor (Fig. 1) is composed of fibrous tissue and spindle-cells, the fibrous tissue predominating in places and in others the spindle-cells.

"There are many areas of cells resembling mucous cells, and to be differentiated from myxomata; vascular supply abundant and vessel walls-formed by tumor-tissue.

"Diagnosis, 'myxosarcoma.'"—Dr. Farquhar Ferguson, Pathologist to the New York Hospital.

CASE II. *Large recurrent sarcoma of the back and groin; entire disappearance of both tumors; patient in perfect health without recurrence four years after the beginning and more than three years after the cessation of treatment.*—This patient was a male, aged forty years, with a sarcoma of the back (lower lum-

bar region) 7x4 inches, with a secondary tumor the size of a goose-egg in the groin. The groin-tumor had been removed in January, but rapidly recurred. The patient was examined by Dr. William T. Bull, who regarded the case as inoperable sarcoma. The same diagnosis was made by a number of other surgeons. The tumor (Fig. 2) was photographed by Dr. George H. Fox, and a section was removed under cocaine and examined by Dr. Farquhar Ferguson, pathologist to the New York Hospital, and the diagnosis confirmed. A full history of the case has already been published.[1] Treatment was begun

FIG. 3.



CASE II.—Sarcoma of back and groin. Well three and a quarter years after treatment.

in the erysipelas-wards of Bellevue Hospital in April, 1892, and daily local injections of living bouillon-cultures of erysipelas were given for two weeks before an attack of erysipelas was produced. The attack was very severe, but during the attack and the few succeeding days both tumors entirely disappeared. Recurrence followed in July, and both tumors grew more rapidly than before. The injections were resumed, and between October, 1892, and January 1, 1893, he had four additional attacks of erysipelas, but mild in character.

In December, 1892, he was exhibited before the Surgical Section of the New York Academy of Medicine. The influence upon the tumors was striking, but less marked and more temporary than the first attack. In January, 1893, I removed the recurrent back-tumor, but left the groin undisturbed. After three weeks there was an apparent recurrence in the back, and I began using the toxic products of erysipelas and bacillus prodigiosus, injecting them locally into the groin-tumor. This preparation was the one made by filtering toxins through porcelain. The two toxins were mixed at the time of using.

The tumors quickly disappeared. The injections were discontinued in March, 1893, and the patient has been in perfect health ever since. (A photograph was taken in April, 1896.)[2]

[Copy from Records, N. Y. Hospital Laboratory.]

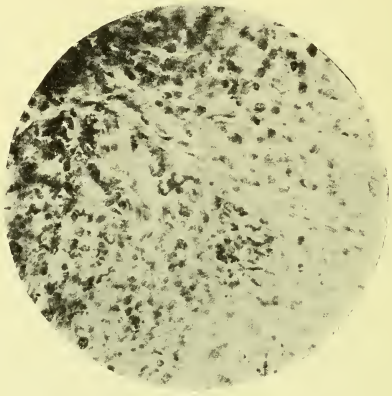
Pathological report. "The tumor (Fig. 4) is a sarcoma, in which the cells are round, oval, and spindle, in which everywhere there is seen a stroma of

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, July, 1894.

[2] September 13, 1896. The patient has a well-marked recurrence in the abdomen. He has rapidly lost flesh and strength the past few weeks.

fibrous tissue, apparently the remains of the subcutaneous tissue which has not been completely destroyed during the development of the tumor. Yellow

FIG. 4.



CASE II.—Sarcoma.

elastic fibres are quite abundant throughout the tumor, but the vascular supply is not very abundant."—Dr. Farquhar Ferguson, Pathologist to the New York Hospital.

CASE III. *Large inoperable sarcoma of the abdominal wall and pelvis; entire disappearance of tumor; no recurrence three years after.*—This case, a boy sixteen years of age, was pronounced inoperable by Dr. L. Bolton Bangs, at the time professor of genito-urinary surgery at the Post-Graduate Hospital. A section of the growth was removed and pronounced spindle-celled sarcoma by Dr. H. T. Brooks, the pathologist to the hospital. Dr. Bangs referred the patient to me for treatment with the toxins, and he was admitted to the New York Cancer Hospital in January, 1892. He was treated for nearly four months with the mixed filtered toxins of erysipelas and bacillus prodigiosus. At the end of this time the tumor had nearly disappeared, and the little that remained was gradually absorbed after the injections were discontinued. There was no breaking-down, and the entire growth disappeared by absorption. The original growth was 7x5 inches in extent, involved apparently the entire thickness of the abdominal wall, was attached to the pelvis, and from symptoms and position evidently involved the bladder-wall. The boy's general condition improved with the disappearance of the tumor, and he has enjoyed the best of health since. He was shown to the members of the New York State Medical Association on October 16, 1895, and was examined by the Medical Board of the New York Cancer Hospital, December 14, 1895. There was no evidence of the tumor remaining. The case is well, May 11, 1896.

Pathologist's report: "Spindle-celled sarcoma."—Dr. Henry T. Brooks, Pathologist to the Post-Graduate Hospital.

CASE IV. *Large inoperable sarcoma of the abdominal wall; entire disappearance; no recurrence two and one-half years afterward.*—This patient was a woman, twenty-eight years of age. An exploratory laparotomy had been performed at the Massachusetts General Hospital, by Dr. Maurice H. Richardson, in August, 1893. The growth was found too extensive to permit of removal, and the wound was closed. A portion of the tumor was removed and examined by the pathologist to the hospital, Prof. W. F. Whitney, of the Harvard Medical School. The diagnosis was "fibro-sarcoma." (Fig. 5.)

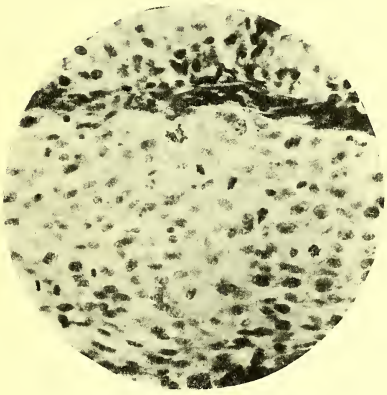
The patient was sent to me by Dr. Richardson in October, 1893, for treatment with the toxins. Local injections of the mixed filtered toxins were given for six weeks; then, after an interval of one month, they were given

for four weeks. At the end of this time only a slight induration remained at the site of the tumor. A few weeks later this also had gone away, and the patient is still in perfect health two and one-half years after, without a suspicion of hardness in the region of the tumor.

In the discussion of my paper before the American Surgical Association, in June, 1894, Dr. Richardson, in reference to this case, said:

"In this case there was no doubt, according to accepted methods of diagnosis, that the woman had a malignant and necessarily fatal disease. The mass filled the right lower quadrant of the abdomen when I operated. I first incised in the median line and came down on the tumor. I then made an incision in the lateral region, with the same result. There was nothing to be done surgically. I took out a section and had it examined. It was pronounced sarcoma. The patient was sent to New York in October. When she came back there was a little induration about the scar. In May there was not the slightest sign that could be detected. Unless the diagnosis was entirely wrong; unless the history, gross appearance, and microscopic examination were entirely wrong, this was a case which must have died sooner or later."

FIG. 5.



CASE IV.—Fibrosarcoma.

August 31, 1893.

"The specimen from the tumor of the abdominal wall was a small, dense, ill-defined, whitish, fibrous-looking mass, which on microscopic examination was found to be made up of large numbers of small cells with a tendency to form fibres. This latter condition was more marked in some places than others. The diagnosis is fibrosarcoma."—Dr. W. F. Whitney, Pathologist to the Massachusetts General Hospital and Curator of the Warren Museum, Harvard Medical School.

[In a personal letter Dr. Whitney states that there was not the slightest doubt of the diagnosis in this case.]

CASE V. *Sarcoma of the leg and popliteal region three times recurrent; disappearance; freedom from recurrence for one and one-half years; then recurrence in the gluteal region.*—This patient, a girl fifteen years of age, had undergone three operations at the New York Hospital, by Dr. William T. Bull. The tumor was a spindle-celled sarcoma, originally starting in one of the metatarsal bones. A Syme's amputation was performed in 1890. Six months later local recurrence appeared in the stump, quickly followed by a second tumor in the popliteal space In January, 1894, the tumor in the popliteal region was the size of a child's head, and the one in the stump the size of a hen's egg. This large

tumor, or as much of it as was possible, was removed by Dr. Bull in January, 1894, but the smaller one was left undisturbed in order to try the effect of the toxins.

The toxins were given at the New York Hospital, under Dr. Bull's direction, for about two months. The tumor of the stump entirely disappeared, and the patient gained seventeen pounds. She was afterward transferred to my service at the New York Cancer Hospital and the injections continued for a time. The indurated mass in the calf slowly disappeared and the patient remained in good health until the last of October, 1895; a tumor of considerable size was then discovered in the right gluteal region, deeply attached, and occupying the space between the greater trochanter and the tuberosity of the ischium. The toxins were resumed, local injections being made into the tumor. There was slow improvement, the most marked features of which were the increase in mobility of the tumor and the more sharply defined outline. There was also some decrease in size. By February, 1896, it was thought that it could be safely removed, and I excised it under ether. The mass was about the size of two fists, deeply attached and partially encapsulated. The wound healed by first intention and the patient is at present in good health.

FIG. 6.



CASE VI.—Spindle-celled sarcoma of scapula and chest-wall, before treatment. Well nearly two years after. Photograph one and a half years after treatment.

Pathologist's report (No. 1845): "Tumor the size of a child's head, measuring 9 x 7 x 4 ½ centimetres, partly surrounded by a smooth capsule, but presents many freshly incised surfaces; whitish in color; very firm; of little vascularity; and presenting the appearance of fibro-sarcoma.

"Microscopic examination of the tumor shows the typical structure of a fibro-sarcoma, with sarcoma elements predominating; vascular supply fairly predominant."—Dr. Farquhar Ferguson, Pathologist, New York Hospital.

[Copy of Records, N. Y. Hospital Laboratory.]

Pathologist's report of tumor removed February, 1896: "Spindle-celled sarcoma."

CASE VI. *Sarcoma of the scapula involving a large part of the left half of the thoracic wall; entire disappearance of the tumor under three months' treatment; patient at present in perfect health without recurrence twenty-three months later.*[1]—The patient was a girl, aged sixteen years, and was admitted to the incurable

FIG. 7.



CASE VI.—Sarcoma of scapula. Photograph nearly two years after treatment.

ward of the New York Cancer Hospital, June 20, 1894. The tumor began in the region of the left scapula, four months before, and at the time the treatment was begun the growth extended to the vertebral line behind, measured thirteen inches vertically, extended around beneath the axilla to the sternum in front. The growth was firmly fixed to the scapula and to the ribs. It was about two inches in thickness in the scapular region. (Fig 6) The skin over it was perfectly normal and movable. The left arm was so bound down by the

[1] A full description of this case will be found in an earlier paper. New York Medical Record, January 19, 1895.

new growth that it could not be raised to the horizontal position. The general condition was much impaired. The mixed unfiltered toxins were injected locally in the scapular portion of the tumor, and continued, with occasional intervals of one or two days, for three months. The improvement was immediate and very striking.

After three weeks the arm could be raised to a vertical position, and in October, 1894, after three months' treatment, the tumor had entirely disappeared by *absorption* only; she has had no treatment since, and remains perfectly well, Sept. 1, 1896. (Fig. 7.) I regard this case as the most remarkable one in the entire series. It was one of the most extensive tumors that I have ever seen, and I hesitated about even making a trial of the toxins, so completely hopeless did it appear. There was no evidence of previous inflammatory, tubercular, or specific trouble, and the diagnosis could scarcely have been questioned even without confirmation by careful microscopic examination; but the examination made from a section nearly an inch long, removed from the thickest part of the tumor by means of a large-sized Mixter punch ($\frac{1}{8}$ inch in diameter), showed it to be typical "spindle-celled sarcoma."

Pathologist's report on section removed from scapular portion of tumor: "Spindle-celled sarcoma."—Dr. H. T. Brooks, Pathologist to N. Y. Post-Graduate Hospital.

CASE VII. *Epithelioma of the chin, lower jaw, and floor of mouth; inoperable; patient well without recurrence two years later.*—This patient, a woman aged thirty-four years, was admitted to the Methodist Episcopal Hospital in May, 1894, with a rapidly growing tumor involving the central portion of the lower jaw, the floor of the mouth, and the soft parts of the chin. There was an area the size of a silver half-dollar upon the chin, which was the seat of a typically epitheliomatous ulcer. A portion was removed and pronounced by the pathologist epithelioma. The tumor had a history of four months' growth. Dr. George R. Fowler regarded the case as inoperable and without hope. He stated that the only operation that could be done would be removal of the lower jaw, floor of mouth, and a part of the tongue; that the risk of death from the operation would be great, and that recurrence within a few months would be almost certain. Dr. Fowler referred the patient to me for treatment with the toxins. In view of the tumor being epithelioma I gave a very bad prognosis, but promised to try the injection.

She was admitted to the New York Cancer Hospital early in June, 1894, and was treated with *mixed toxins unfiltered* (B. prodigiosus and S. erysipelatosus) for about ten weeks. The injections were made into the chin and repeated daily as a rule. In three weeks the ulcerated area had entirely healed, and the diseased portion in floor of mouth had greatly improved

In September, 1894, the patient had become very much run down from the long-continued injections and severe reactions, and two small ulcers one-fourth inch in diameter appeared in the chin. She was sent home to recuperate. Her only treatment since that time was the administration of tonics and local application of electricity to the chin for a short time by Dr. Sarah V. Burnette.

I had a photograph of her taken October 7, 1895. She was examined by a number of surgeons, December 14, 1895. No indication could be detected in the scar nor in the floor of the mouth, and the patient was in perfect health. The patient was quite well in June, 1896.

Pathologist's report: "Material from chin and lower jaw, May 20, 1894. Sections were not entirely satisfactory, but from gross appearance of the materials and those revealed by the microscope the diagnosis of epithelioma is offered."—William N. Belcher, M.D.

Dr. Fowler, in a letter enclosing the pathologist's report, states:

"While I am sure that the case was one of epithelioma, judging from the clinical standpoint, and based upon the history of its rapid growth as well as its recurrence upon removal, yet I am fully aware that epithelial findings, from every standpoint, should be absolutely beyond question. Dr. William

N. Belcher, pathologist to the Methodist Episcopal Hospital, and member of the Brooklyn Pathological Society, made the report, and in a letter explaining his report he states: 'The fragments were frozen by the use of the carbon-dioxide apparatus, and free-hand sections made. Notwithstanding the unsatisfactory picture revealed by the microscope, there seemed to me to be sufficient to warrant the opinion that the material was of an epitheliomatous character. Upon consulting the hospital records, I find that the diagnosis of epithelioma was made by the operating surgeon, presumably prior to my report, and it would seem to me to be as nearly correct as any diagnoses can be.'"

FIG. 8.



CASE VII.—Epithelioma of chin and floor of mouth. Before treatment.

FIG. 9.



Same patient one and a half years after treatment. Patient well two years.

This case is presented as fairly as possible, and the profession may form its own judgment as to its value.

CASE VIII. *Recurrent epithelioma of the face.*—The patient, aged forty-five years, male, had a small recurrent epithelioma of the face involving the lower eyelid. The primary tumor I had removed by operation, at the New York Cancer Hospital, eighteen months before, and microscopic examination by Dr. E R. Dunham proved the growth to be epithelioma. Although the tumor in this case was not extensive, its removal by operation would have necessitated enucleation of the eye, and since he had lost the other eye in youth, I decided to try the toxins before sacrificing the eye. The recurrent tumor was treated at the hospital in February and March, 1895. The growth apparently entirely disappeared, and the patient had had no return up to January, 1896.

Case IX.—E. I., female, aged twenty-three years, born in Switzerland, lived in the United States for six years. In May, 1894, she had a pain in the right hypochondriac region. Attacks of pain became more and more frequent and severe, and in August, 1894, were so bad that the patient was confined to bed. Operation, German Hospital, August 16, 1894, by Dr. Willy Meyer: Exploratory laparotomy; tumor was found apparently springing from the mesentery, but attached to the omentum and the gall-bladder. It was found impossible to remove it, but a portion was excised for examination and abdomen closed. In September, 1894, she was sent to me by Dr. Meyer for treatment with the toxins. At the time there remained a sinus at the centre of the abdominal incision, discharging a thin, viscid fluid. Palpation showed an intra-abdominal mass beneath the cicatrix about four inches in diameter. General condition fair. She was put upon the treatment with the mixed toxins of erysipelas and bacillus prodigiosus, injections being made sometimes in the abdominal wall, sometimes in the buttocks. The injections were given at intervals of every other day, and continued with occasional intervals, until February 7, 1895. There still remained a small sinus at the site just above described, and only an indistinct resistance remained at the site of the tumor. General health seemed perfect. She was readmitted to the hospital in order to attempt to close the sinus, which persisted, and at times became blocked up and caused considerable pain and discomfort. Two attempts were made to close the sinus under ether, the last in September, 1895. An incision carried down to the peritoneum enabled one to make a very thorough examination of the contents of the abdomen, but failed to discover the presence of a tumor. The cicatricial tissue about the sinus was carefully excised and the wound allowed to heal from the bottom. The peritoneum was not opened. Patient was discharged from the hospital on October 12th, sinus still persisting. Examination on January 25, 1896, showed the sinus closed; there was no distinct tumor present, but there was some induration in the region of the cicatrix, which apparently had increased since her discharge from the hospital on October 12th.

Operation, March 4, 1896. An incision three inches long was made at the site of the old cicatrix, and the sinus was followed up until it entered a closed pouch containing two to three ounces of muco-purulent fluid. By carefully enlarging the incision the finger was introduced and the pouch proved to be the gall-bladder. Several calculi about one-half inch in diameter were found tightly wedged in the cystic duct. These were dislodged with great difficulty and the cavity of the gall-bladder drained with iodoform-gauze. The peritoneum was opened for a distance of about one inch and quickly closed with catgut sutures. The most careful examination of the patient failed to reveal the slightest evidence of the tumor which was present at the time of Dr. Meyer's operation one and one-half years before.

In a letter describing his operation, Dr. Meyer states:

"At the physical examination previous to operation, in August, 1894, there was a small, irregular swelling on the outer side of the right rectus muscle about two fingers' width above McBurney's point. On entering the abdominal cavity I found a hard, irregular infiltration, which involved the omentum, ascending colon, loop of small intestine, and the border of the liver, matting together all these parts. Clinically the disease impressed me, as also everybody present, as a malignant growth, probably sarcoma. To define clearly its origin was impossible; it seemed to start from the omentum, as this was especially involved. To remove the growth radically seemed impossible. I also had not the permission of the relatives of the patient to do any major—perhaps here fatal—operation, which latter, in order to be radical, would have to consist in a resection of a portion of the large as well as of the small intestine, and also of a portion of the liver, besides the omentum. I therefore removed a wedge-shaped piece of the growth for microscopic examination and closed the wound in the tumor by two catgut stitches. I regret now not having palpated at that time the gall-bladder,

but a primary disease of the latter, probably due to the presence of gall-stones, did not enter my mind at all. Microscopic examination of the piece removed was made by the pathologist of the German Hospital, Dr. F. Schwyzer, who at that time pronounced it to be round-cell sarcoma Permit me to congratulate you on the outcome of this very interesting and important case."

Case X. *Sarcoma of the spine.*—Miss H , aged twenty-eight years, had a small tumor situated about half-way between the right breast and axilla, removed a year and a half ago. It was pronounced benign by the surgeon, but it is doubtful whether a microscopical examination was made. A year ago she began to develop a small swelling in the spine, about the tenth dorsal vertebra. It was supposed to be due to beginning Pott's disease, and was treated accordingly. In June she consulted Dr. V. P. Gibney, of New York, who considered the diagnosis of Pott's disease as probable, and treated her for some time with a plaster jacket. The jacket caused increase rather than decrease of the pain; the swelling slowly but perceptibly increased in size, and her general health became very much impaired. In December, 1894, the tumor had become of such size, and the pain so severe, that the theory of Pott's disease was given up, and a diagnosis of sarcoma of the spine was no longer doubtful. The patient was referred to me by Dr. Gibney, with the idea of trying the toxin treatment if the condition of the patient would permit. When I examined her the middle of December, in consultation with Dr. William Maddren, of Brooklyn, she had been bedridden for several months, and was very much emaciated. Her lower extremities were completely paralyzed, and numerous bedsores were present over the sacrum and ilium. Her heart-action was very feeble and rapid, and her urine contained albumin and casts. Over the lower dorsal region there was a fusiform swelling about six inches in length, the outlines of which were poorly defined. The tumor was absolutely fixed to the spine, so much so that it seemed an enlargement of the spine itself. A peculiar œdematous condition of the skin was present both over the tumor and the entire lower extremities. The condition of the patient was so desperate that I advised against attempting the treatment. A few weeks later, at the urgent request of the family and the attending physician, Dr. Maddren, I began giving very small doses The treatment was continued by Dr. Maddren; the injections were given sometimes every day, and others at intervals of two days, and kept up for one month. At the end of one month I again saw the case, and the improvement was nothing less than wonderful. The peculiar œdema above referred to had almost entirely disappeared; the tumor itself had diminished very markedly in size; the patient was able to move both legs; the bedsores had taken on a healthy appearance and had partially healed, and the general condition in every way had markedly improved

The improvement continued until April, 1895, when the bedsores had healed; the patient had regained control over the bladder and rectum, and was able to stand upon her feet and walk a few steps with support No further improvement occurred, and in May, 1895, she began to get worse, and slowly failed until August, 1895, when she died. Before death other tumors developed in different parts of the body, rendering the diagnosis certain. Two small recurrent tumors in the region of the breast at the site of the original tumor disappeared under the injections of the toxins, although the injections were given in the back.

Case XI. *Sarcoma of iliac fossa; partial disappearance.*—The patient, aged fifty-five years, was born in Ireland, and had nothing worthy of note in his family or previous history. In January, 1893, he noticed a swelling in his right iliac region. It was accompanied by some pain, and grew steadily in size.

When I first saw him, in June, 1893, when he was admitted to the New York Cancer Hospital, there was a tumor about the size of two fists deeply seated in the right iliac fossa. There was marked pulsation, which was regarded as transmitted, and the tumor was diagnosed as sarcoma. An

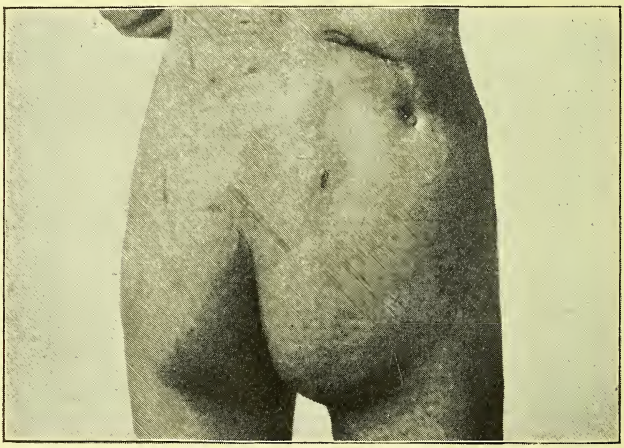
exploratory incision was made, extra-peritoneal, and a portion removed, and the diagnosis confirmed.

Injections of the erysipelas and prodigiosus toxins were at once begun, and continued with occasional intervals the greater part of the entire year. The tumor slowly decreased in size, and at the present time the greater part of it has been absorbed. The patient was in good health one year after treatment, and then lost sight of.

CASE XII. *Spindle-celled sarcoma of palm of hand, six times recurrent; treated with the toxins with temporary success; tumor recurred one year later.*[1]—A rapidly growing sarcoma of the palm of the hand had been held in check for a year and a half by injections of the mixed toxins given at intervals during this period. In June, 1894, the treatment was pushed for three weeks, at the end of which time the necrosed tumor-tissue was removed under ether. No further treatment was given and the patient regained twenty pounds of lost weight. She remained well until August, 1895, when she had a local recurrence, and amputation of the forearm was performed by Dr. Samuel Lloyd. The patient now shows signs of recurrence in the brain.

CASE XIII. *Very large osteo-chondrosarcoma of ilium; disappearance of tumor; recurrence seven months later.*—This case is one of great importance on account of the size as well as the character of the neoplasm. A full history of the case has been published in the paper referred to (*loc. cit.*), and only the main points will be noted here. The patient was a man, twenty-

FIG. 10.



CASE XIII.—Very large osteo-chondrosarcoma of ilium.
Photograph taken seven months after successful treatment with the mixed toxins.

three years of age, with a tumor of one year's duration, occupying a larger portion of the right ilium, and extending from the middle of the sacrum behind to the border of the right rectus in front, filling up the larger portion of the right iliac fossa. He was much emaciated and rapidly losing ground. I saw the patient at the request of Drs. George F. Shrady and F. Kammerer, under whose charge he was, at St. Francis's Hospital The toxins were begun in March, 1894, and continued under my direction for five weeks. Marked reactions followed the injections (mixed filtered toxins). The tumor after a few days began to soften and break down, and a large area of fluctuation appeared. Free incision permitted the escape of much broken-down tissue and large masses continued to slough out for a considerable time.

[1] The full history of this case may be found in a former paper. New York Medical Record January 19, 1895.

High temperature continued for a month after the injections were stopped, due to the absorption of dead tissue. At the end of this time improvement began, and he rapidly regained his health and strength. By November 15, 1894, the tumor had apparently entirely disappeared and the patient had gained twenty-nine pounds since August, fully forty pounds since June, and had resumed his work. He was shown before the Surgical Section of the

FIG. 11.



CASE XIII.—Recurred eight months after treatment. Photograph one and a half years after.

New York Academy of Medicine, and Dr. Shrady regarded him as cured. In December, 1894. there was evidence of local recurrence, and in spite of further treatment with the toxins the tumor has steadily increased in size up to the present time. His condition is hopeless, though he is able to walk about with a cane.

No microscopical examination of the original tumor was made, but the rapid growth and enormous size made the diagnosis clear, while the recurrence and prospective fatal issue confirm it. The patient died in July, 1896.

CASE XIV. *Recurrent angiosarcoma of the breast treated with erysipelas-serum* —A. C., female, aged fifty-nine years, United States. Family history good. Seventeen years ago she was hit upon the left breast by a little boy of seven years; three months later at the site of the blow there appeared a small lump; this grew slowly, was accompanied by some pain, and at the end of three years had reached the size of a fist. The first operation was then performed (fourteen years ago) at St. Francis's Hospital. The breast was not removed, and there were no enlarged glands in the axilla. She remained free from recurrence for seven years, when a tumor recurred, grew slowly for two years, and was then operated upon a second time at the same hospital, by Dr. George F. Shrady (May, 1889); the tumor at this time was the size of an egg, and the diagnosis made by Dr. Shrady was sarcoma. She again remained free from disease for two years, when a tumor recurred *in situ*. Examination January 20, 1895, showed a large tumor occupying the region of the left breast, extending from the anterior axillary line to the sternum, and from just below the clavicle nearly to the free border of the ribs. The tumor was fairly well fixed to the chest-wall, and was markedly protuberant, made up of more or less distinct nodules, the surface of which was purple in color, and in places there was considerable ulceration with foul discharge. The tumor was unquestionably inoperable. The patient's general condition was so extremely weak that she was scarcely able to walk alone. She was admitted to the New York Cancer Hospital on

January 20, 1895, and placed in the "incurable" ward. The disease was so far advanced and the general condition was so bad that no attempt was made to give her the toxins. After the ulcerated surface had become somewhat less foul under careful treatment, and her general condition a little improved, she was placed under treatment with injections of the antitoxin-serum of

FIG. 12.

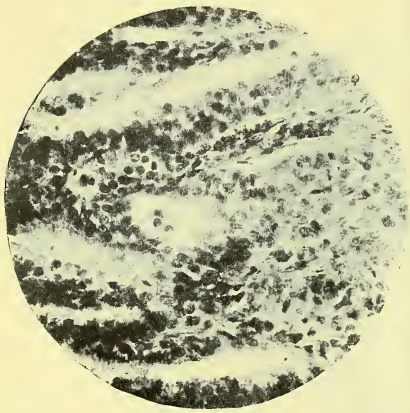
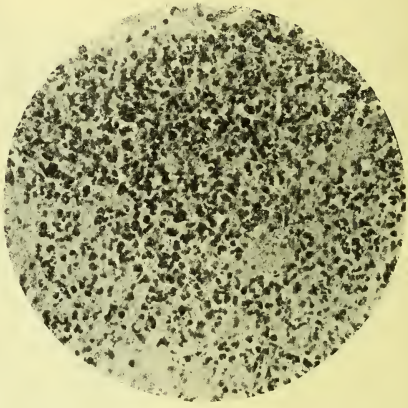


FIG. 13.



CASE XIV.—Angiosarcoma of the breast.

erysipelas and bacillus prodigiosus. This serum was prepared by Mr. Buxton in a manner similar to the diphtheria-serum—the toxins of erysipelas and prodigiosus having been injected daily into a horse for about six weeks, and the serum then withdrawn.

Effect of the injections. In small doses of 5 to 10 minims very little effect was noticed. Larger doses, 15 to 20 minims, frequently caused intense mus-

FIG. 14.

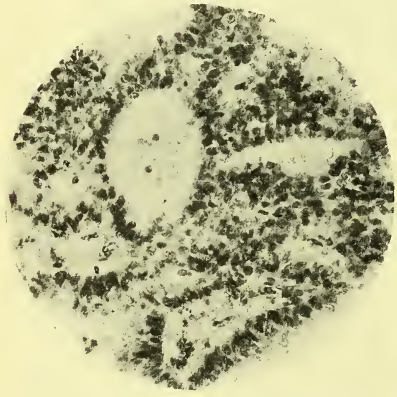
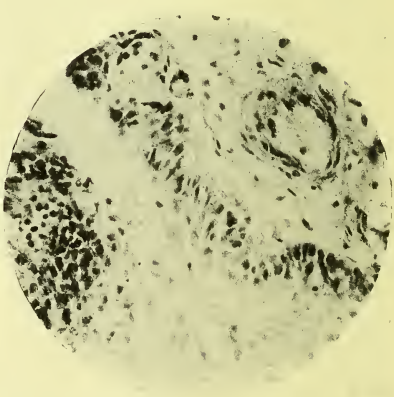


FIG. 15.



CASE XIV.—Angiosarcoma of the breast.

cular pain and an urticaria-like condition of the skin, sometimes extending over the whole back and chest, being the cause of intense itching and discomfort. Patient also complained of very severe headaches, lasting sometimes for several days. The dose was never carried beyond 20 minims, but was, as a rule, given daily. The tumor soon began slowly to decrease in size, and

became much more movable; the general condition of the patient likewise slowly improved. Treatment was continued, with occasional intervals, until September, 1895. At this time the tumor had become so small that it could be easily removed by operation, and not having shown any great diminution in size during the past month, it was deemed advisable to remove it. Ether given, a mass was removed. The periosteum of the ribs was not involved, but as the skin over the tumor was diseased, a large area, four by six inches, was left to heal by granulation. No further treatment was given; the ulcer healed over as rapidly as could be expected, and on December 14th it had entirely healed. There were a few small glands, about one-fourth of an inch in diameter, in the left axilla, but, as the glands on the opposite side were even more enlarged, no attempt was made to remove them. Patient was discharged from hospital the latter part of December, 1895. Examination January 30, 1896, showed the patient in good general condition; no evidence of recurrence found.

Microscopical examination by Prof. T. M. Prudden. "I have examined a large number of sections from different parts of the tumor of breast, and, although there is considerable diversity in detail of the said growth in different parts, I think that the structures are all referable to the type of angio-sarcoma, which accordingly is the anatomical diagnosis." (Figs. 12, 13, 14, and 15.)

CASE XV. *Recurrent spindle-celled sarcoma of the palm of hand; entire disappearance.*—Miss M , aged eighteen years; family history good; injured right hand two years ago. In July, 1895, noticed a small swelling in the palm of the right hand. In October, 1895, it had reached the size of half a hickory-nut, and was removed. The wound suppurated and was seven weeks in healing; it recurred very quickly, and a second operation was performed by Dr. Edward Martin, of Philadelphia, on January 2, 1896. Microscopical examination of the parts removed at the first operation showed it to be sarcoma. The palm of the hand was split open and the tumor found to consist of a thickening in the sheaths of the tendons; apparently the tumor was confined entirely to the sheaths of the tendons; the thickened sheaths were dissected out and the wound closed. The swelling, when Dr. Martin first saw it, was the size of a half dollar, irregular, indurated, slightly raised, and attached to the tendon. Microscopical examination of the tissues removed showed it to be a spindle-celled sarcoma.

Examination on February 15, 1896, showed in the centre of the palm of the right hand a cicatrix 2½ inches long; underneath this was a mass extending the entire length of the cicatrix, one and one-half inches wide at the centre, attached to the skin, and apparently to the tendons, but not fixed to the bony structures; the outline was not well defined. Just above the wrist, along the flexor tendons, was another small mass, about 1 inch in diameter and slightly raised above the surrounding parts. Injections of the mixed toxins of erysipelas and bacillus prodigiosus, filtrate, were begun on the 15th of February, 1896, 2 minims being given, followed by slight headache; no febrile reaction. On February 16th, 1 minim of the unfiltered toxins was given; temperature 100½°; slight headache. February 18th, 1½ minims of the unfiltered toxins were given, producing a chill lasting half an hour; temperature 101½°; good deal of headache. On the 19th 1½ minims of the unfiltered toxin caused a very severe chill, beginning half an hour after injection; temperature rose to 103°; pulse 160; very severe headache, feeling of bursting of vessels in the head. On the 21st 2 minims of the filtrate were given.

Examination on February 21st showed the mass in palm of the hand very much smaller and much more movable; mass in the wrist has also diminished in size. No local inflammation at the point of injections.

The injections were continued, usually daily, until March 30th. The mass in the palm of the hand had nearly disappeared; the fingers could then be straightened voluntarily; when treatment was begun the fingers could not be extended beyond 120 degrees The gland in the region of the epicondyle was hardly perceptible. During the last two weeks the injections were made

in the arm entirely, a filtered solution of the mixed toxins being used, and the largest dose being 20 minims.

The treatment was continued for six weeks by the patient's brother, a physician, all the injections being made in the arm. Examination, May 15, 1896, showed the tumor had entirely disappeared and she was able perfectly to extend fingers. She was presented to the New York Surgical Society, May 27, 1896.

CASE XVI. *Probable sarcoma of sacrum; entire disappearance; well one year later.*—H. B. H., male, thirty-eight years of age; born in Ireland and lived in the United States twenty years. Family history good; personal history: always well In February, 1895, he began to lose flesh and strength, and soon after began to have pain in the lower part of the spine over the region of the sacrum; a little later pain began to shoot down the legs, more marked upon the right; consulted Dr. W. C. Deming, of Westchester, on April 1, 1895. At that time he was beginning to be slightly lame in the right leg; soon after some lameness appeared in the left leg as well. All these symptoms progressively increased; pain was very acute, so much so that the patient expressed a wish to die. On the 2d of May he was sent by Dr. Deming to St. Luke's Hospital. His normal weight of 175 pounds had fallen to 134 pounds. He was so lame that it took him more than one hour to walk from Forty-second to Fifty-fourth Street (a little more than half a mile). He was admitted to Dr. Francis P. Kinnicutt's service, who, on careful examination of the rectum, found a tumor attached to the anterior portion of the sacrum, the lower border of which could be reached with the index finger; the tumor was of firm consistence and fixed to the sacrum; extent of the tumor upward could not be determined as it was inaccessible. The patient was emaciated and his general appearance was very suggestive of malignant disease. The diagnosis of Dr. Kinnicutt and the other physicians and surgeons who saw him in consultation was: inoperable sarcoma.

On May 10th I was asked to see the patient in consultation with Dr. Kinnicutt, and the conditions found were such as above described; my diagnosis was the same as Dr. Kinnicutt's. I advised a trial of the toxins for two or three weeks, but if no improvement should be noticed by that time I advised discontinuance of the treatment. The injections with the mixed unfiltered toxins were begun at once, and made into the buttocks; the treatment was repeated daily and at the end of one week the pain had almost entirely subsided and the lameness had markedly improved The treatment was carried out at St Luke's Hospital for six weeks; at the end of that time the improvement was so great that the patient returned to his home and on the last of June resumed his work. The injections were continued by Dr. Deming two to three times a week, and were given in the evening and did not interfere at all with his usual occupation. By the end of June—seven weeks after the treatment had begun—the patient had gained 28 pounds in weight, and stated that he felt as well as ever.

Examination on March 8, 1896, shows the patient apparently in perfect physical health; he has no lameness whatever and no trace of his tumor can be detected on rectal examination. His present weight is 175 pounds. He has had no treatment for several months.

The report of this case I owe to the courtesy of Dr. Kinnicutt and Dr. Deming, for although the treatment was carried out under my direction I did not personally have charge of the case.

CASE XVII. *Fibro-angioma of the upper lip.*—J T., born in Germany, aged thirty-two years; occupation farmer. Was operated upon in Chicago, by Dr. Andrews, in 1892, later by Dr. French, for present trouble. Family history absolutely negative. Since birth has had a thick upper lip, not growing much until twenty-one years old, when lip was thick as little finger and grew very slowly until four years ago, when it began to grow rapidly. Physical examination showed tumor size of a very large orange, involving the entire upper lip, being about nine inches from one corner of mouth to the other. Tumor pulsated synchronously with heart-beats, and was of same

temperature as rest of body. It projected over lower lip to level with tip of chin

Operation, November 4, 1895, by Dr. Robert T. Morris, of New York. Tumor transfixed with long narrow scalpel, the handle being used as a hare-lip pin and a figure-of-eight gauze bandage thrown around same; greater part of tumor was then excised.

Two weeks after operation the condition of the patient was as follows: The whole base of the upper lip was occupied by a tumor one inch thick on the right side, extending upward $1\frac{3}{4}$ inches; on the left side the tumor was thinner, about $\frac{1}{2}$ inch in thickness, and extending upward one inch. The toxins were begun the middle of November, 1895; injections were made into the dense tissue of the tumor about one inch from the lower border. The tumor immediately began to decrease in size and at the end of three weeks had almost entirely disappeared. Dr. Morris then performed a plastic to restore the lip, and in a letter recently received the patient states there has been no return of the disease. Microscopic examination of the tumor showed it to be a fibro-angioma.

Case XVIII. *Tumor of sternum, tubercular; rapid degeneration under the toxins; disappearance; no return in one and one-half years.*—This case was fully reported January 19, 1895 (loc. cit.), but it is of sufficient importance to note here the subsequent history. The case was reported as a "probable sarcoma," although no positive diagnosis was made by Dr. Ferguson The tumor was firm in consistence, three inches in diameter, and occupied the upper third of the sternum. It was of four months' duration, and the patient had two sisters suffering from cancer. After one week's treatment the tumor had almost entirely broken down.

Sinuses persisted for several months, and examination of the discharge from the sinuses made by Dr. E. K. Dunham, pathologist to the New York Cancer Hospital, in January, 1895, showed the presence of tubercle bacilli, therefore proving the original tumor to have been probably tubercular in character.

It is of considerable interest to note that a second tumor of apparently similar nature in the left lumbar region, extending over upper part of ilium, underwent rapid degeneration during the injections of the toxins into the sternal tumor; but this was followed by a sinus that failed to close.

The curative influence of accidental erysipelas in *scrofula* was referred to at some length in a very important monograph entitled *Etude Clinique sur influences curative de l'Erysipèle dans la Syphilis*, by Charles Mauriac, published in Paris in 1873, nearly ten years before either the germ of erysipelas or that of tuberculosis had been discovered. Among the conclusions formulated by Mauriac we find this: "The curative influence of erysipelas exercises itself upon all these lesions however remote," showing that he clearly recognized both the local and systemic character of this peculiar action. Very recently Dr. Robert H. Green, of New York, has begun to investigate the action of the mixed toxins of erysipelas and bacillus prodigiosus.

Erysipelas-serum. The experiments with erysipelas antitoxic serum have, with one exception, been followed by negative or very slight results, and have been abandoned. A combined erysipelas and diphtheria antitoxic serum has been tried in two cases of carcinoma, but with little appreciable effect.

Continued experiments verify the opinion before expressed that the

mixed unfiltered toxins of erysipelas and bacillus prodigiosus form the most effective preparation thus far used.

The investigations of Park[1] in diphtheria show that the amount of toxins in the filtrate is not more than one-half of the total amount contained in the liquid culture, and the same is probably true in erysipelas-cultures.

The value of the toxins depends entirely upon the virulence of the culture, and it is extremely difficult to keep the culture up to the requisite standard of virulence. This will explain in great measure the varying results.

Since the last paper, published over a year ago, there has been no change in the methods of preparing the toxins. Cultures have been made in bouillon containing varying quantities of peptone and of various degrees of acidity and alkalinity, but nothing has so far been found better than the ordinary neutral peptone-bouillon.

In preparing the serum the mixed unfiltered toxins were injected subcutaneously into a horse every two or three days for two months, beginning with 5 c.c. and running up to 100 to 120 c.c. As a rule, a rise of temperature of two or three degrees, lasting for several hours, would follow each injection, whilst locally there would be œdema and swelling without formation of pus, the swellings persisting for several days and appearing painful to the touch. The horse was finally bled from the external jugular vein and the serum prepared in the way recommended for diphtheria-antitoxin.

TABLE I.—TUMORS WHICH ENTIRELY DISAPPEARED AFTER TREATMENT, SHOWING THEIR NATURE AND FINAL RESULT.

	Free from recurrence in	No.	Recurred in	No.	Total.
Sarcoma, spindle-celled	4, 3, 2¾, 2, and ½ years.	5	1½ and 1 years.	2	7
" round-celled	2 and 1 years.	2		0	2
" mixed-celled	3½ years.	1		0	1
Chondrosarcoma		0	8 months.	1	1
Osteosarcoma	1 year.[2]	1	7 "	1	2
Epithelioma	2 years.	1	15 "	1	2
Carcinoma	3 months.	1		0	1
Total		11		5	16

[1] Journal of Experimental Medicine, January, 1896.

[2] No microscopal examination was made of this tumor, which was clinically diagnosed as osteosarcoma of the sacrum (*vide* text).

TABLE II.—SHOWING THE KINDS OF TUMORS TREATED, AND THE RESULT.

	Totally disappeared.	Totally disappeared, but recurred	Improved.	Unimproved.	Died.	Prophylactic injections only.	Total.
Sarcoma, spindle-celled	5	2	7	...	...	...	14
" round-celled	2	...	16	31	3	...	52
" mixed-celled	1	...	1	1	...	...	3
"	...	...	4	4	...	...	8
" melanotic	...	...	2	5	...	...	7
Myxosarcoma	...	...	2	2	...	...	4
Chondro-osteosarcoma	...	1	1	...	...	...	2
Osteosarcoma	1	1	...	2	...	...	4
Cylindroma	...	...	1	1	...	...	2
Carcinoma	1	...	10	23	...	4	38
Epithelioma	1	1	5	15	...	1	23
Malignant, nature not known	...	...	4	6	...	...	10
Total	11	5	53	90	3	5	167

Successful Cases by Other Surgeons Employing this Method.

CASE I.—Dr. Johnson's case of extensive spindle-celled sarcoma of the palate and fauces, extending down to the vocal cords, disappeared entirely under local injections of the mixed, filtered toxins. The case was published in full in the *New York Medical Record*, November 17, 1894. The patient is at present in perfect health, without recurrence, two and one-half years after treatment. The diagnosis of spindle-celled sarcoma was confirmed by microscopic examination. I saw the case in consultation with Dr. Johnson, and can bear witness to the hopeless, inoperable condition prior to treatment.

CASE II.—Dr. John E. Owens, attending surgeon, St. Luke's Hospital, Chicago, has sent me a very complete history of a case of sarcoma of the tibia, successfully treated with the toxins:

The patient, a boy, aged seven years, had received an injury to his leg in July, 1894. In December, 1894, a swelling appeared in the upper portion of the tibia. In March, 1895, exploratory operation was performed, showing a tumor involving the medullary canal. Microscopic examination was made by Dr. E. R. LeCount, of the department of pathology of the Rush Medical College. His report was as follows:

"The pieces of tissue show that they were removed from a myeloid or giant-celled sarcoma, originating from the bone; they are very hemorrhagic, showing not only free hemorrhage into the sarcomatous tissue, but, also, large blood-spaces are very numerous. I should judge this to be a rapidly growing tumor; its malignancy is unquestioned."

Dr. Owens writes: "Before the use of the mixed toxins amputation above the knee would have been at once performed."

The treatment was begun on April 10, 1895, and continued until July 10, at intervals of one to two days. The affected leg had become almost normal in size; the difference in circumference of the two being only one-half inch.

Dr. Owens writes: "When the patient left the city I was led to the conclusion, from the favorable condition of the leg, that a recovery had taken place. At all events, I thought it best to discontinue the toxins and resume them should the limb again present an unfavorable appearance."

The patient was again seen on November 16, 1895, when the scar seemed somewhat elevated, although Dr. Owens did not think that the sarcoma had begun to reappear; further injections, however, were advised as a precaution, but the family decided against resuming the treatment.

In this case Dr. Owens's conclusions were as follows:

"When the treatment with the toxins was discontinued the patient had very much improved in general health; sleep, which before had been very much disturbed, was now all that could be desired. The leg presented a most favorable appearance. I felt gratified that a cure had been effected; and even if some recurrence had occurred, the further use of a remedy which had exercised such a powerful influence would, in my opinion, have brought the case to a successful issue."

CASE III. *Spindle-celled sarcoma of the calf of the leg; entire disappearance under twelve weeks' treatment with the mixed toxins.*—Dr. L. L. McArthur, attending surgeon, St. Luke's Hospital, Chicago, in connection with Dr. Owens, have sent me the following report:

The patient, female, aged forty years, without any family or previous history worthy of note, entered St. Luke's Hospital for the removal of a tumor of the leg. Operation revealed a tumor springing from the dense fascia covering the muscles of the calf. Although a very radical operation was performed, the patient was informed of a probable recurrence, and advised that, if any return were noted, to have an immediate amputation. She re-entered St. Luke's Hospital seven months later with a recurrence in the cicatrix and a tumor, the shape and size of half an egg, bulged from the calf of the leg. Having, in the meantime, tried the mixed toxins on another case, I determined to try them here, partly because the patient was three and one-half months pregnant. Treatment was continued for twelve weeks, with the result of a slow and steady disappearance of the tumor. Patient returned to the maternity ward seven months later; there had been no recurrence. Microscopic examination showed the growth to be a spindle-celled sarcoma.[1]

CASE IV. *Osteosarcoma of the lower end of the radius; three times recurrent; entire disappearance of the tumor under three months' treatment with the mixed toxins.* A second case reported by Dr. McArthur.

"The patient was admitted to the Michael Ress Hospital for recurrence in the cicatrix of a bony tumor, situated in the lower end of the right radius. The patient stated that the growth removed had been pronounced sarcoma by Dr. Christian Fenger, and amputation having been refused the tumor had been removed as thoroughly as possible. Three to four months later a recurrence followed, and he was reoperated upon by Dr. Wyllys Andrews, by the same method. The same diagnosis was made. Speedy recurrence followed. He then consulted Dr. D. A. K. Steele, who advised amputation of the arm. This the patient refused, and thereupon consulted me. I advised amputation, which was refused. I then agreed to try the toxins. After twelve weeks' treatment the growth had entirely disappeared. Three months later I presented the patient to the Chicago Medical Society for examination. I regret that no microscopic examination had been made in the case."

CASE V. *Round-celled sarcoma of the orbit; marked improvement.*—Dr. McArthur has sent me notes of a third case worthy of brief mention.

A little girl, five and one-half years old, with large, round-celled sarcoma of the antrum of Highmore, extending into the nose, nasal pharynx forming a hard falx, producing extensive exophthalmus; cervical glands markedly enlarged, both anterior and posterior to the sternal mastoid muscle; she was brought to St. Luke's Hospital from Iowa. She had emaciated to thirty-seven pounds; was advised not to make the journey, as she would probably die on the train. She was brought to the hospital on a pillow in an almost moribund condition. After stimulants, tonics, and rectal feeding had been employed for three days, the administration of the toxins was begun; the injections were given every other day, and at the end of two weeks the patient was eating heartily, walking about, and riding on street cars, etc. There was a perceptible diminution in the exophthalmus. Believing I could aid the toxins, I removed the enlarged glands. Examination showed them to be

[1] In April, 1896, Dr. McArthur writes me there is a slight suspicion of recurrence.

typically sarcomatous. Three weeks later I removed the contents of the antrum, nasal cavity, extending back to the spino-maxillary fascia. The wounds healed primarily; cavity of the antrum was drained for six weeks. The patient was sent back to her home weighing sixty-nine pounds. She was advised to continue the treatment under the direction of her family physician. Getting very intense reactions, the physician discontinued the treatment. Recurrence followed not long after. Treatment was resumed with the result that she again began to improve. The improvement, however, did not continue, and two months later the patient died.

CASE VI.—*A case of extensive inoperable intraperitoneal sarcoma* was successfully treated by Dr. Mynter, of Buffalo, and reported in full in the *New York Medical Record*, February, 1895.

Dr. Mynter writes me under date of May 21, 1896:

"One of my assistants met the patient last week in excellent health; she had had no return of the disease, and you may safely report her as well to date."

The diagnosis of this case was confirmed by exploratory laparotomy and microscopical examination.

CASE VII.—Dr. R. Tilly, of Chicago, under the direction of Dr. McArthur, treated a case of round-celled inoperable sarcoma of the orbit with the mixed toxins. The tumor entirely disappeared. The patient, a short time afterward, died suddenly, when apparently cured. There was no autopsy.

CASE VIII.—Dr. Thomas F. Rumgold treated a case of eight times recurrent round-celled sarcoma of the breast, with the result of entire disappearance of the tumor. The patient died a few weeks later. Autopsy revealed extensive internal metastases. The case was reported as under treatment in an earlier paper.

CASE IX.—Drs. R. M. Stone and C. C. Allison, of Omaha, Neb., have just sent me a complete history of a successful case of inoperable malignant tumor of the uterus. There was marked infiltration of the right broad ligament, and the disease was regarded as too far advanced for hysterectomy. The patient had lost fifteen pounds in weight. Cervix had been removed by operation. At the time when the toxins were begun the patient was suffering from repeated hemorrhages, and three surgeons who saw her in consultation regarded the case as absolutely hopeless. The toxins were begun on December 4, 1895, and given at first in the scapular region, and later in the tumor itself. Improvement was very marked and rapid. On January 29, 1896, the tumor had apparently disappeared and the patient was able to be up and about. She is, at the present time, in perfect health. A number of sections of the tumor were examined by Dr. W. R. Lavender, Professor of Pathology at the Omaha Medical College. Diagnosis of spindle-celled sarcoma was made.

This case will shortly be published in full by Dr. Stone.

CASE X —Dr. M. Storrs, of Hartford, Conn., has recently sent me a report of a case of large inoperable spindle-celled sarcoma of the axilla, which has entirely disappeared under four months' treatment with the toxins. The patient was seen in consultation by a number of surgeons, and the case was regarded as entirely inoperable and hopeless. Portions of the tumor were removed at three different times, and microscopic examination showed it to be a spindle-celled sarcoma. A section of the tumor has been examined by the pathologists of the New York Cancer Hospital, and also by Professor William Welch, of the Johns Hopkins Medical School, and the diagnosis was confirmed. This case is, of course, too recent to be looked upon as a cure, but the fact that this large, inoperable tumor, with a diagnosis of spindle-celled sarcoma demonstrated beyond question, has totally disappeared under no other treatment than the mixed toxins, must be regarded as strong evidence that these toxins exert a specific influence on such tumors.

CASE XI.—Dr. Sydney W. Wilcox[1] reports a case of myxosarcoma of the

[1] North American Journal of Homœopathy, January, 1896.

hand treated with the mixed toxins from June until August, 1895. The tumor nearly disappeared under the treatment. Dr. Wilcox states in a letter of April 10, 1896, that there has been no apparent return.

CASE XII.—Dr. J. Flippen, of Thomasville, N. C., has sent me notes of a case of rapidly recurrent sarcoma of the arm. The patient was a physician, seventy-four years of age. During one year he had undergone twenty operations, the tumor recurring after each operation with greater rapidity. When the toxins were begun the largest tumor was the size of a fist. After the injections had been given for two weeks this tumor had diminished to the size of a filbert, and the patient's general condition was markedly improved. At the time when the injections were begun he was confined to his bed; after two weeks' treatment he was able to go about and attend to his practice. He was told by other physicians that the injections were dangerous, and was advised to abandon the treatment. The disease remained quiescent for about three weeks, then the tumor began to increase in size rapidly. Amputation at the shoulder-joint was performed. Three to four weeks later the tumor recurred in the scapular region and quickly caused his death.

CASE XIII.—Czerny[1] gives his experience concerning the treatment of malignant tumors with the injections of the mixed toxins of erysipelas and bacillus prodigiosus in eight cases, four of which were sarcoma and four carcinoma. One case of inoperable round-celled sarcoma of the parotid was cured. It was a rapidly growing tumor of five months' history, occupying the entire region of the right parotid gland, extending back of the ear, and giving complete facial paralysis. The tumor was the size of a man's fist at the time when the treatment was begun. After eighteen injections had been given in the course of six weeks, the tumor had dwindled to three soft nodules, movable in the skin, and all measuring about one and a half by one-half inches. In a letter written May 20, 1896, Czerny states that he afterward excised the small portions of the tumor that remained, and the patient is at the present time quite well. This is the only case in which he has had complete success.

CASE XIV. *Carcinoma of the breast, with very marked improvement.*—Dr. George T. Howland, of Washington, D. C., had under his care a case of carcinoma of the breast, in which the treatment was partially successful. The patient, aged sixty-two years, had a typical carcinoma of the left breast, which was first noticed in September, 1894. In February, 1895, examination showed a tumor involving the major portion of the left breast, being six and one-half inches in the long diameter and four and one-half in the short. It was firmly adherent to the chest-wall; the skin was infiltrated and adherent; axillary glands were enlarged to the size of a hazelnut. A section of the tumor was removed with a Mixter punch for microscopical examination, which showed it to be a scirrhous carcinoma. The treatment with the toxins was begun February 10, 1895, and continued until May, 1895. On Februray 23, 1895, the tumor measured two and one-half by four and one-half inches, having decreased two inches in either direction. It had become freely movable upon the chest-wall. The axillary glands had decreased to the size of a hazelnut. In other words, the tumor had become easily operable, and operation was advised but refused by the patient. During May and June, within which time no injections were given, the tumor increased in size. The injections were again tried for a short time with little apparent effect. She continued to grow worse and died on the 22d of February, 1896.

Dr. Howland's conclusions are: "That the toxins exerted a beneficial effect upon the growth, as proved by the measurements given; by the manner in which the tumor was released from its firm adhesions to the chest-wall; by the decrease in the size of the axillary glands; marked changes in consistency; and by the cessation of the pain."

CASES XV. and XVI. Very recently[2] Dr. Henry Matagne, of Bruxelles, has

[1] Muenchener medicinische Wochenschrift, September 3, 1895.

[2] Gazette Médicale de Liége, May 14, 1896.

reported a case of cure of an epithelioma of the floor of the mouth. No microscopic examination was made, but the submaxillary glands were enlarged and the diagnosis was confirmed by several prominent physicians, who advised operation, but the patient refused to have an operation performed. The treatment was begun January 10, 1895, and lasted about three months. Dr. Matagne also reports a second successful case of recurrent sarcoma of the neck, the size of an egg, that totally disappeared under three and one-half months' treatment with the mixed toxins. Six months later there was a slight return. A third case of recurrent sarcoma of the neck the size of a fœtal head decreased two-thirds under three months' treatment with the toxins. The patient then consulted a surgeon. The operation proved fatal.

Dr. Matagne used the toxins in three other cases of sarcoma with slight effect, and also in eight cases of carcinoma with very little result.

It is quite true that most of the successes reported by other observers are as yet too recent to be fairly classed as cures, and such is not my object in presenting them. Whether they recur or not, they furnish the strongest possible evidence of the antagonistic and specific influence of the toxins upon inoperable sarcoma, and, in connection with my own cases that have passed the three-year limit, we have proof that such influence may be curative.

It would be hardly possible to expect the profession at large to accept without question or criticism such startling results as I have reported; hence I have related with some detail the successful results of others who have employed this method.

This series of upward of twenty cases of inoperable sarcoma, four of which have remained well for more than two and one-half years, the diagnosis in all of which has been established beyond question, according to the accepted methods of diagnosis, I believe to be sufficient to demonstrate that a real and positive step forward has been made in a field that, up to the present, has resisted every attempted advance of medical science.

I am conscious that there are men who will remain skeptical as to the value of the toxins *in spite* of the evidence here presented. They either fail to see any logical connection between the action of accidental erysipelas and the toxins, or they even go so far as to deny that there are any authentic cases of malignant tumors that were cured by accidental erysipelas. The only explanation they have to offer for these results, which cannot be questioned, is that in all of the successful cases there must have been an error of diagnosis.

Such an explanation might be entitled to some consideration were only a single case involved, but to propose it seriously as a satisfactory explanation of the result in twenty cases is, I believe, unworthy of anyone who claims to be guided by scientific principles. Much has been made of the spontaneous disappearance of tumors supposedly malignant. I have made a careful study of the reported cases of this kind, and have failed to find a *single* instance of a tumor disappearing spontaneously or after exploratory operation in which the diagnosis of sarcoma or carcinoma had been confirmed by microscopical examination.

On June 23, 1894, this subject was most thoroughly discussed before the Royal Medical and Chirurgical Society of London, when Greig Smith read a paper upon the "So-called Disappearance of Abdominal Tumors." At that discussion, Mr. Bland Sutton stated that he did not believe in the spontaneous disappearance of any connective tissue or cancerous growths, and the spontaneous disappearance of myomata which had been recorded as based on clinical observation alone. It would be somewhat remarkable that these cases I have reported should be the first and thus far the only ones with both clinical and microscopic diagnosis of malignancy to disappear spontaneously, and it would be more remarkable still that this disappearance should be coincident with the beginning of the treatment with the toxins.

It would be clearly unfair to rule out these cases on the ground of error in diagnosis, without ruling out the cases of cure following operations for sarcoma. Both have been subjected to the same standards of diagnosis, and the cases treated by the toxins have been subjected to more severe tests, inasmuch as in many of the cases the clinical and microscopical diagnoses were confirmed by a number of the best surgeons and pathologists.

Space will not permit entering into a discussion of the theories that have been advanced in explanation of the action of the toxins upon malignant tumors. I will merely say that I still adhere to the opinion expressed at some length in an earlier paper (1892, *loc. cit.*) that the micro-parasitic origin of malignant tumors furnishes the most rational ground for any satisfactory explanation of the action of the toxins.

The evidence in favor of this theory is steadily increasing, and I believe that in the near future it will amount to positive proof. If this theory be correct, it is quite possible that the unequal action of the toxins upon the different types of sarcoma may be due to slightly varying types of the organism that produces the tumor. The recent and most valuable researches of Dr. Thayer at the Johns Hopkins Hospital have shown that the different types of the malarial organism produce different types of disease, which are by no means uniform in their power of resisting the action of a specific remedy.

Metchnikoff,[1] in 1892, called attention to the close analogy existing between the parasite of malaria and the coccidia, and regarded it as significant that carcinoma should closely approximate the category of miasmatic affections, as proved by its endemic character.

The conclusions that I have drawn from a careful study of this series of cases may be briefly expressed as follows:

1. The mixed toxins of erysipelas and B. prodigiosus exercise an antagonistic and specific influence upon malignant tumors, which influence in a certain proportion of cases may be curative.

[1] British Medical Journal, December 10, 1892, p. 1273.

2. This influence is slight in most cases of carcinoma (including epithelioma); most marked in sarcoma, but varies with the different types, the spindle-celled form showing by far the greatest influence.

3. The action of the toxins is not merely local in character, but systemic.

4. The toxins should be used only in clearly inoperable cases, or after primary operation to prevent recurrence.

5. The results will vary greatly with the strength of the preparation, the most virulent cultures giving the best results.

I desire to express my very great obligations to Mr. B. H. Buxton, Director of the Loomis Laboratory and Assistant Pathologist to the New York Cancer Hospital, who has spent much valuable time in preparing the toxins. I am also much indebted to Dr. E. K. Dunham, the Pathologist to the New York Cancer Hospital and Director of the Carnegie Laboratory, for the micro-photographs.

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